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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/730,323	BOLLA ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	WS

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-41 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-41 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 2/22/2007 in which claims 29-37 and 39-41 were amended. Claims 29-41 and 43 are pending and under examination in the instant Office action.

Drawings

The drawings were received on 2/22/2007. These drawings are acceptable.

Claim Objections

The amendment to claim 36 is acknowledged and found remedial. The objection to claim 36 is hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 31-32, 37 & 39-41, and therefore dependent claims 30, 33-36, 38 & 43, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which Applicant regards as the invention. **These rejections are maintained IN PART for reasons of record, and are new only where necessitated by Applicant's amendment.**

Claim 29 recites "[a] transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast under control of a yeast derived promoter, said nucleic acid polymer being selected from the group consisting of synthetic and natural nucleic acid polymers, said nucleic acid polymer having a sequence that codes for expression of two or more amino acid residues in a ratio that offsets a deficiency in a predetermined feed source for a target animal, the deficiency being that the predetermined feed source presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" in lines 1-10 (emphasis added). Claim 29 is vague and indefinite in that the metes and bounds of a "yeast derived promoter" are unclear. What characteristics of the promoter must remain in order for the promoter to be yeast derived? Does Applicant intend a promoter isolated from yeast, or does Applicant intend a promoter which is derived from yeast, but which comprises one or more substitutions, deletions, additions or insertions?

Claim 29 is also vague and indefinite in that the metes and bounds of a feed source that "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" are unclear. The terms "optimal" and "efficient" are relative terms that render the claim vague and indefinite. The terms "optimal" and "efficient" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Does Applicant intend a predetermined feed source which is deficient in that it comprises amino acids in a ratio which stunts the target animals growth and/or prevents the target animal from gaining weight (and thus does not allow for "efficient" use of any and all proteins), or does Applicant intend, e.g., such a feed source which comprises amino acids in a ratio that simply prevents the target animal from gaining as much weight as it might otherwise gain if more efficient use of the protein source present in the predetermined feed source could be made by the target animal?

Similarly, claim 37 also recites a feed source that "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the

target animal" in lines 7-8. Claim 37 is vague and indefinite as explained for claim 29, above.

Claim 31 recites "[t]he transformed yeast strain of claim 29, wherein said nucleic acid polymer is inserted into said strain's chromosome" in lines 1-2 (emphasis added). Claim 31 is vague and indefinite in that "said strain's chromosome" lacks clear and positive antecedent basis. Does Applicant intend such a method wherein the nucleic acid polymer is inserted into said strain's *genome*, or does Applicant intend to insert the nucleic acid polymer into a particular chromosome of the strain?

Claim 32 recites "[t]he transformed yeast strain of claim 29, wherein said polypeptide is held by said strain" in lines 1-2 (emphasis added). Claim 32 is vague and indefinite in that it is not clear what "held by" means. Does Applicant intend a transformed yeast cell of claim 29, wherein said polypeptide is not secreted, or does Applicant intend such a yeast cell wherein the polypeptide is stable within the cytoplasm of the yeast cell, or both?

Claim 39 recites "[t]he construct of claim 37 wherein said polypeptide comprising Lysine, Methionine/Cysteine; Threonine; Valine; Isoleucine; histidine; and Tryptophan amino acid residues in a ratio that is about 6:3:1:2:6:1" in lines 1-4 (emphasis added). Claim 39 is vague and indefinite in that it

is unclear whether Applicant intends a polypeptide comprising lysine, a sulfur-containing residue which is either methionine or cysteine, threonine, valine, isoleucine, histidine and tryptophan in a ratio of 6:3:1:2:6:1, respectively; or whether Applicant intends a polypeptide comprising lysine, either methionine or cysteine (but not a mixture of both), threonine, valine, isoleucine, histidine and tryptophan in a ratio of 6:3:1:2:6:1, respectively?

Similarly, claims 40 and 41 recite polypeptides comprising "Methionine/Cysteine" residues in a particular ratio with other residues. Claims 40 and 41 are vague and indefinite as explained for claim 39, above.

Response to Arguments

With regard to the rejection of claim 29 under 35 USC 112, 2nd paragraph as vague and indefinite because the term "yeast derived promoter" is unclear, Applicant argues that lines 29-31 of page 11 of the specification state that the promoter is preferably isolated from the organism to be transformed as opposed to being synthesized chemically. Thus, Applicant argues, the yeast derived promoter as claimed may be isolated from yeast. Applicant further argues that the methodology for isolation of yeast promoter DNA may be readily found in the

literature publicly available at the time the instant Application was filed. Applicant further argues that Applicant is not required to disclose what is well known in the art. Therefore, Applicant argues, the term "yeast derived promoter" is not vague or indefinite.

Applicant's arguments have been carefully considered and are respectfully found unpersuasive. Although Applicant's specification does teach at page 11, lines 29-31, that "[i]t is preferred if the promoter is isolated as opposed to synthetic" and that the promoter "be derived from the organism that is to be transformed," Applicant's specification does not define the metes and bounds of a promoter "derived" from yeast or the steps involved in the deriving. Furthermore, Examiner agrees with Applicant insofar as the promoter may be isolated from yeast, but Applicant has not claimed a promoter isolated from yeast, rather one which is "derived" from yeast and which reasonably can be interpreted to include any number of mutations, insertions, deletions or additions. Moreover, while Applicant is not required to describe what is well known in the art, this argument is not germane to the instant rejection; the instant rejection is appropriate because Applicant has failed to distinctly claim and particularly point out the subject matter which Applicant regards as the invention, not because Applicant

has failed to offset any deficiencies in the prior art with regard to what Applicant's invention is.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-41 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record.**

Response to Arguments

Applicant argues: "As amended, the ratio of amino acids in the polypeptide encoded by the construct of Claim 37-41 or expressed by the transformed yeast strains of Claim 29-36 are governed by the dietary need of the animal which is in turn controlled by the nature of the animal, the particular feed

source selected" (see page 6, 1st full paragraph or the Remarks filed 2/22/2007). Applicant further argues that the specification provides ample showing of how the dietary requirements may be determined. Applicant further argues that the prior art along with the instant Application provide ample teaching by which the composition of the polypeptide can be determined. In support of this assertion, Applicant points to portions of the specification which describe how a cereal grain may be selected, how the amount and ratio of amino acids required to be supplemented may be determined and further how the specification provides examples of amino acids requirements by three different species. Applicant also argues that "[t]he nutritional needs of a given animal and the amino acids content of a given feedstock may be readily determined by consulting standard veterinary and animal science handbooks" (see page 6, last paragraph of the Remarks filed 2/22/2007). Therefore, Applicant asserts, all the limitations of claims 29-41 and 43 are adequately described in the specification and one of skill in the art would recognize that Applicant was in possession of the invention at the time the instant Application was filed.

Applicant's arguments have been carefully considered but are respectfully found unpersuasive. Applicant's argument that "[a]s amended, the ratio of amino acids in the polypeptide

encoded by the construct of Claim 37-41 or expressed by the transformed yeast strains of Claim 29-36 are governed by the dietary need of the animal which is in turn controlled by the nature of the animal, the particular feed source selected" is not found persuasive because the claims as amended still encompass a whole genus of constructs and transformed yeast cells which encode a peptide that is defined by its ability to offset a deficiency in a predetermined feed source for a target animal. Applicant's argument that the ratio of amino acids is governed by the dietary need of the animal, which is in turn controlled by the nature of the animal and the particular feed source selected, neither narrows the genus of encompassed polypeptides/amino acids nor provides any structural information with regard to the encompassed polypeptides. Similarly, Applicant's argument that the prior art and the specification provide teachings for how the composition for such a polypeptide should be determined also is not persuasive because description of the nutritional needs of a given animal and the amino acid content of a given feedstock are not adequate support for claims which are drawn to nucleic acid constructs and/or yeast cells transformed with such a construct wherein the normally exogenous polypeptide encoded/made by the construct/yeast cell includes two or more amino acid residues that offset a deficiency in a

predetermined feed source for a target animal. As explained in the previous Office action mailed 9/22/2006, the examples in the specification are only representative of one such transformed yeast strain and the results are not predictive of any other yeast trains/nucleic acids constructs capable of being produced by a yeast such that the ratio of amino acids, when added to a predetermined feed source offsets a deficiency in the predetermined feed source, said deficiency being that the predetermined feed source presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gamin of the target animal. In fact, depending upon the feed source and the target animal, the claims would seem to encompass any yeast strain transformed with a construct comprising any yeast derived promoter operably linked to any peptide comprising two or more amino acid residues which is ordinarily exogenous to the yeast, of which myriad are present in the prior art. Given the very large genus of nucleic acid molecules/transformed yeast encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the nucleic acid sequences capable of fulfilling the claim limitations of claims 29-41 and 43, the skilled artisan would not have been able to describe the broadly claimed genus of nucleic acid constructs, transformed yeast

comprising such a construct, or methods of use of such contructs such that the amino acid ratio offsets a deficiency in a predetermined feed source, wherein the deficiency in the feed source is such that amino acids are presented in a ratio that is less than optimal for efficient use of protein for growth and weight gain of the target animal. Thus, the skilled artisan would have reasonably concluded Applicant was not in possession of the claimed invention for claims 29-41 and 43.

Claims 35 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection. This is a new rejection necessitated by Applicant's amendment.**

The specification as originally filed does not provide support for the invention as now claimed: a transformed yeast comprising a nucleic acid polymer encoding a polyepeptide "whereby said nucleic acid polymer when expressed produces a polypeptide comprising methionine, histidine, lysine, threonine, isoleucine, valine and tryptophan residues in a ratio that is

about 3:6:6:2:2:1:1" (claim 35); or "whereby said polypeptide comprising Lysine, Methionine/Cysteine; Threonine; Valine; Isoleucine; histidine; and Tryptophan amino acid residues in a ratio that is about 6:3:2:1:2:6:1" (claim 39), or "wherein said polypeptide comprising Lysine and Methionine/Cysteine residues in a ratio that is about 10:3" (claim 40); or "wherein said polypeptide comprising Lysine; Methionine/Cysteine; Arginine; and Histidine residues in a ratio that is about 10:2:10:3" (claim 41). The specification does not provide sufficient blazemarks nor direction for the instant polypeptides encompassed by the above-mentioned limitations, as currently recited. The instant specification instead discloses ratios of amino acids that "approximate the needed essential amino acids in corn based diets" (see, e.g., page 29, lines 4-8 and Table 1). These ratios are designed such that "the need for lysine" is "set equal to 100" (ibid). The specification also discloses an expressed polypeptide "comprised of 3 methionine, 6 histidine, 6 lysine, 2 threonine, 2 isoleucine, 1 valine, and 1 typtophan residues" or "units" (see page 8, 2nd full paragraph and page 15, lines 6-9). The instant claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present

claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 29-30, 32-34, 36-37 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Barr et al (*J. Exp. Med.* **165**:1160-1171, 1987). **This is a new rejection NOT necessitated by Applicant's amendment.**

Note: For purposes of this rejection only, the intended use of the nucleic acid polymer for expression of two or more amino acid residues in a ratio that offsets a deficiency in a

predetermined feed source for a target animal, wherein the deficiency in said predetermined feed source is such that it "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter as long as the protein is comprised of two or more amino acids. This is because any such yeast cell could fulfill the claim limitations wherein upon addition to a feed source, the polypeptide would offset a deficiency in efficiency of protein use, the deficiency being defined as the lack of the protein being supplemented, whatever that protein may be.

Barr et al teach a transformed yeast strain (*Saccharomyces cerevisiae* strain AB110) comprising two different nucleic acid polymers (pAB24/P.vivax-1 and pAB24/P.vivax-2) for encoding a polypeptide ordinarily exogenous to yeast (*P. vivax* circumsporozoite protein antigens) under the control of a yeast derived promoter (an ADH-2/GAPDH promoter hybrid), said nucleic acid polymers being synthetic in that 1) pAB24/P.vivax-1 comprises sequences excised from pUC9 plasmids and ligated to "synthetic adapters" and 2) pAB24/P.vivax-2 was constructed "using the Nco-1/Ban-1 fragment from vivax-1 together with

synthetic DNA encoding amino acids Glu 307 to Leu 335" (see entire document, especially page 1161, Figure 1 and paragraph bridging pages 1161 and 1162). With regard to claim 30, the expression of the polypeptide is inducible upon growth in culture medium comprising 1% glucose (see page 1162, lines 23-24 where Barr et al teach that "[f]or induction and analysis of vivax-1 CS protein, yeast cells were diluted 1:20 into medium containing 1% glucose and were grown for 36 h at 30°C" (emphasis added) as well as page 1163, last paragraph). With regard to claim 32, Barr et al teach such a transformed yeast strain wherein said polypeptide is "held" by said strain, because Barr et al were able to isolate the polypeptides from yeast extracts (see page 1164, Figure 2; paragraph bridging pages 1164-1165; and page 1165, Figure 3). Regarding claims 33, Barr et al also teach such a transformed yeast strain wherein said strain is auxotrophic, but was non-auxotrophic prior to transformation (see page 1162 wherein Barr et al teach that pAB24 contains URA3 and LEU2 markers "for selection of *ura* or *leu* yeast auxotrophs in uracil- or leucine-deficient media"). With regard to claim 36, the promoter is a GAPDH hybrid promoter (see page 162, lines 6-11). Finally, with regard to claim 43, Barr et al also teach a method for producing a yeast additive comprising inserting such a construct into a yeast strain and expressing the gene in

said construct (see above as well as Barr et al at paragraph bridging pages 1161-1162 and 1164-1165, Figures 2 and 3).

Claims 29-30, 32-34, 36-37 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Nussenzweig et al (US Patent No. 4,826,957) as evidenced by Barr et al (*J. Exp. Med.* **165**:1160-1171, 1987; cited above). **This rejection is maintained for reasons of record, but also contains new grounds of rejection not necessitated by Applicant's amendment.**

Note: For purposes of this rejection only, the intended use of the nucleic acid polymer for expression of two or more amino acid residues in a ratio that offsets a deficiency in a predetermined feed source for a target animal, wherein the deficiency in said predetermined feed source is such that it "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter as long as the protein is comprised of two or more amino acids. This is because any such yeast cell could fulfill the claim limitations wherein upon addition to a feed source, the polypeptide would offset a deficiency in efficiency of protein use, the deficiency

being defined as the lack of the protein being supplemented, whatever that protein may be.

Nussenzweig et al teach a transformed yeast strain (*Saccharomyces cerevisiae* strain AB110) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (*P. vivax* circumsporozoite protein antigen) under the control of a yeast derived promoter (an ADH-2/GAPDH promoter hybrid), said nucleic acid polymer being a synthetic polymer (see entire document, especially Example 1 at column 9, lines 40-45; and column 10, lines 9-68). The construct for insertion into the yeast is referred to as "pAB24/*P.vivax1-5*" (see column 10, line 62). With regard to claim 30, the expression of the polypeptide is inducible upon growth in culture medium comprising YEP with 1% glucose (see paragraph bridging columns 10-11). This is evidenced by Barr et al who teach the same ADH-2/GAPDH hybrid promoter can induce expression of a *P. vivax* protein upon growth in medium containing 1% glucose at page 1162, lines 23-24: "[f]or induction and analysis of vivax-1 CS protein, yeast cells were diluted 1:20 into medium containing 1% glucose and were grown for 36 h at 30°C" (see page 1162, lines 23-24 and page 1163, last paragraph; emphasis added). With regard to claim 32, Nussenzweig et al teach such a transformed yeast strain wherein said polypeptide is "held" by said strain

because Nussenzweig et al were able to isolate the polypeptides from yeast extracts as confirmed by Western blotting (see column 11, lines 2-37 and Figure 4). Regarding claims 33, Nussenzweig et al also teach such a transformed yeast strain wherein said strain is auxotrophic, but was non-auxotrophic prior to transformation (see column 10, lines 43-53). With regard to claim 36, the promoter is a GAPDH hybrid promoter (see, e.g., column 10, lines 28-36). Finally, with regard to claim 43, Nussenzweig et al also teach a method for producing a yeast additive comprising inserting such a construct into a yeast strain and expressing the gene in said construct (see above as well as Nussenzweig et al at column 10, lines 59-68 and column 11, lines 1-19).

Claims 29-32, 34, 36-37 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Tully et al (US Patent No. 6,337,193). **This rejection is maintained for reasons of record, but has been slightly modified in order to accommodate Applicant's amendment.**

Note: For purposes of this rejection only, the intended use of the nucleic acid polymer for expression of two or more amino acid residues in a ratio that offsets a deficiency in a predetermined feed source for a target animal, wherein the

deficiency in said predetermined feed source is such that it "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter as long as the protein is comprised of two or more amino acids. This is because any such yeast cell could fulfill the claim limitations wherein upon addition to a feed source, the polypeptide would offset a deficiency in efficiency of protein use, the deficiency being defined as the lack of the protein being supplemented, whatever that protein may be.

Tully et al teach a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially Figures 2 & 5; column 2, lines 5-12 & 20-28; column 3, lines 18-36; and column 5, lines 40-45). Tully et al teach such a strain wherein the expression of the polypeptide is inducible, i.e., wherein the production of the MBP protein is under the control of the AOX1 promoter which is inducible by methanol (see, e.g., column 5, lines 20-25). With

regard to claim 31, Tully et al now anticipate Applicant's amended claim because Tully et al teach the use of integrative vectors which recombine into the yeast genome, i.e., one or more of the chromosomes of the transformed yeast (see column 5, lines 60-67). Regarding claim 32, the polypeptide produced by the transformed yeast is "held" by the transformed yeast insofar as transformed cells that secret the protein would "hold" the protein for a given period of time before the protein is released into the culture medium. Regarding claim 34, the transformed yeast strain is *Pichia pastoris* (see, e.g., column 2, line 26-28). Regarding claim 36, the promoter utilized for the production of PDI is the GAPDH promoter (see, e.g., column 5, lines 15-45). Regarding claim 37, Tully et al also teach the construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism under the control of a yeast derived promoter, wherein the nucleic acid polymer is a plasmid and is used to make a protein that would be capable of offsetting a deficiency in predetermined feed source wherein the deficiency in the predetermined feed source is such that it presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal (see, e.g., Figures 2 & 5; column 2, lines 5-12 & 20-28; column

3, lines 18-36; and column 5, lines 40-45). Tully et al also teach a method for producing this yeast additive comprising inserting such a construct into a yeast strain and expressing the gene (see, e.g., Example 3, columns 11-14).

Claims 29-30, 32, 34, 36-37 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheng et al (US Patent No. 5,985,605). **This rejection is maintained for reasons of record, but has been slightly modified in order to accommodate Applicant's amendment.**

Note: For purposes of this rejection only, the intended use of the nucleic acid polymer for expression of two or more amino acid residues in a ratio that offsets a deficiency in a predetermined feed source for a target animal, wherein the deficiency in said predetermined feed source is such that it "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter as long as the protein is comprised of two or more amino acids. This is because any such yeast cell could fulfill the claim limitations wherein upon addition to a feed source, the polypeptide would

offset a deficiency in efficiency of protein use, the deficiency being defined as the lack of the protein being supplemented, whatever that protein may be.

Cheng et al teach a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (*Selenomonas ruminantium* JY35 phytase) under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially Figures 15; column 5, lines 54-58; column 3, lines 66-67 through column 4, lines 1-15; and column 7, lines 44-65). Cheng et al teach such a strain wherein the expression of the polypeptide is inducible (see, e.g., column 9, lines 11-36). Regarding claim 32, the polypeptide produced by the transformed yeast is "held" by the transformed yeast insofar as the transformed cells may or may not secrete the exogenous protein (see, e.g., column 7, lines 57-59). Regarding claim 34, the transformed yeast strain is *P. pastoris* or *S. cerevisiae* (see, e.g., column 7, line 44-49). Regarding claim 36, a promoter utilized for the production of phytase is the GAPDH promoter (see, e.g., column 8, lines 9-18). Regarding claim 41, Cheng et al also teach a method for producing this yeast additive comprising inserting such a

construct into a yeast strain and expressing the gene (see, e.g., column 12, lines 56-67 and column 13, lines 1-9).

Claims 29-34, 36-37 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Lei (US Patent No. 6,451,572). **This rejection is maintained for reasons of record, but has been slightly modified in order to accommodate Applicant's amendment.**

Note: For purposes of this rejection only, the intended use of the nucleic acid polymer for expression of two or more amino acid residues in a ratio that offsets a deficiency in a predetermined feed source for a target animal, wherein the deficiency in said predetermined feed source is such that it "presents amino acids in a ratio that is less than optimal for efficient use of protein for the growth and weight gain of the target animal" is interpreted by Examiner to encompass any transformed yeast cell which expresses a heterologous protein under the control of a yeast derived promoter as long as the protein is comprised of two or more amino acids. This is because any such yeast cell could fulfill the claim limitations wherein upon addition to a feed source, the polypeptide would offset a deficiency in efficiency of protein use, the deficiency being defined as the lack of the protein being supplemented, whatever that protein may be.

Lei teaches a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (see, e.g., the appA gene of *E.*coli at column 5, lines 63-64) under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially column 5, lines 45-67; column 6, lines 33-37; and column 8, lines 9-56). Regarding claim 30, Lei teaches such a strain wherein expression of the polypeptide strain is inducible (see, e.g., column 8, lines 11-36). Regarding claim 31, Lei teaches such a strain wherein the polymer may be inserted into the host strains genome, i.e. one of the strain's chromosomes (see column 7, lines 39-41). Regarding claim 32, the polypeptide produced by the transformed yeast is "held" by the transformed yeast insofar as the transformed cells do not secrete the exogenous protein (see, e.g., column 7, lines 19-24). Regarding claim 33, the transformed yeast cell is auxotrophic, but was non-auxotrophic prior to transformation, as would be the case with the use of URA3 as a selectable marker (see, e.g., column 8, lines 50-56). Regarding claim 34, the transformed yeast strain is *S. cerevisiae* (see, e.g., column 6, lines 3-37). Regarding claim 36, a promoter utilized for the production of phytase is the GAPDH promoter (see, e.g., column 8, lines 9-18). Regarding

claims 37, Lei also teaches the construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein the nucleic acid polymer is a plasmid and used to make a protein that would be capable of complementing a deficiency in predetermined feed source when added in quantity to the predetermined feed source for consumption by the target animal (see, e.g., column 7, lines 36-67 and column 8, lines 1-28). Regarding claim 43, Lei also teaches a method for producing this yeast additive comprising inserting such a construct into a yeast strain and expressing the gene (see, e.g., Example 4 at column 16 and Example 7 at column 20).

Response to Arguments

Applicant argues that the Nussenzweig et al, Tully et al and Cheng et al references do not anticipate the claims as amended, because "[c]laims 29, 37 and 43, as amended, are specifically limited to yeast cells or DNA construct or use therof, that contain a gene encoding a polypeptide with amino acid content of said polypeptide being determined by the desired quantity and ratio of amino acids for dietary requirements of the animal" (see page 7, 1st full paragraph of the Remarks filed 2/22/2007). Applicant further argues that the Nussenzsweig et

al, Tully et al and Cheng et al references do not teach "the claim limitation of determining the amino acid requirement of an animal fed with a particular grain" (see page 7, 2nd full paragraph of the Remarks filed 2/22/2007). With regard to the Lei et al reference, Applicant noticed that Examiner mistakenly cited the patent number and provided the patent number of the Cheng et al reference instead; Applicant therefore requested clarification with regard to this rejection.

Applicant's arguments have been carefully considered but are respectfully found unpersuasive. Applicant's assertion that the claims as amended, now limit the transformed yeast and construct for insertion into said yeast to one containing a gene encoding a polypeptide with amino acid content of said polypeptide being determined by the desired quantity and ratio of amino acids for dietary requirements of the animal is not found persuasive because, with no limitation of what the feed source deficiency is and with no limitation with regard to the polypeptide composition except that it must "offset" the predetermined feed source's deficiency, any transformed yeast cell comprising a nucleic acid construct with a yeast derived promoter operably linked to a sequence encoding a polypeptide of two or more amino acids anticipates the rejected claims. Furthermore, Applicant's argument that the Nussenzsweig et al,

Tully et al and Cheng et al references do not teach the claim limitation of determining the amino acid requirement of an animal fed with a particular grain is not persuasive because this is not a limitation of the present claims. In order to anticipate the claims, a reference need only teach a transformed yeast cell comprising a nucleic acid construct with a yeast derived promoter operably linked to a sequence encoding a polypeptide of two or more amino acids as explained above. Nowhere in Applicant's instant set of claims is a method step for determining the amino acid requirement of an animal fed with a particular grain even recited. With regard to the Lei reference (US Patent No. 6,451,572), Examiner acknowledges the mistaken citation to US Patent No. 5,985,605 and has corrected the rejection under 102(e) as anticipated by Lei (US Patent No. 6,451,572) accordingly.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29-34, 36-38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lei (US Patent No. 6,451,572, cited above) in view of Sikorski et al (*Genetics* **122**:19-27, 1989, cited previously). **This rejection is maintained for reasons of record but has been slightly altered in order to accommodate Applicant's amendment.**

As explain above, Lei teaches a nucleic acid construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein the nucleic acid polymer is a plasmid and is used to make a protein that would be capable of

offsetting a deficiency in predetermined feed source (see, e.g., column 7, lines 36-67 and column 8, lines 1-28). Lei also teaches a method for producing this protein comprising inserting such a construct into a yeast strain and expressing the gene (see, e.g., Example 4 at column 16 and Example 7 at column 20). Regarding the use of vector, Lei teaches that the vector can be any vector that replicates autonomously or integrates into the genome of the yeast. Lei also teaches that the promoter may be a glyceraldehydes-3-phosphate dehydrogenase promoter (see column 7, last paragraph and column 8, first full paragraph). Lei also teaches the use of vectors which carry URA3 as a selectable marker.

Lei does not teach such a construct wherein said construct is a pRS316 plasmid with a GAPDH promoter.

Sikorski et al teach the use of the pRS316 plasmid for expression of proteins in yeast. Sikorski et al teach that pRS316 comprises the URA3 selectable marker and that such a vector has the advantage that "in addition to the general features afforded the pRS vectors by the pBLUESCRIPT backbone, such as ssDNA production, high plasmid DNA yields and extensive polylinker, unidirectional deletion formation and simplified cloning (blue/white screening for recombinants), these new vectors offer unique yeast-specific features," i.e., the pRS316

vectors "allow one to perform almost all routine yeast DNA manipulations in the same plasmid" (see page 25, 2nd column, first full paragraph). Sikorski et al also teach that the streamlined design of the pRS vectors makes them well suited to serve as the starting point for construction of other yeast vectors (see entire document, especially paragraph briding pages 24-25 and page 25, second column, first full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the pRS316 vector as taught by Skorski et al with the GAPDH promoter as taught by Lei, because Lei teaches the use of any yeast vector for production of a heterologous protein in yeast and further teaches the use of a GAPDH promoter for expression of the protein and the use of a URA3 selectable marker;Sikorski et al teach that pRS316 is a useful vector for maninupaltion of DNA (such as cloning) and expression of proteins in yeast and that it comprises a URA3 selectable marker.

One would have been motivated to substitute the pRS316 vector as taught by Sikorski et al in the methods taught by Lei, including the use of the GAPDH promoter, because Sikorski et al teach that the streamlined design of the pRS vectors would make DNA manipulations and cloning easier and Lei teaches that the

use of the GAPDH promoter for strong production of a heterologous protein in yeast and the URA3 marker for selection.

Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when utilizing the pRS316 yeast vector as taught by Sikorski et al in the methods and constructs as taught by Lei.

Response to Arguments

Applicant has requested clarification on the Lei reference which was inadvertently cited improperly (see above). Examiner apologizes for the mistake and has correctly cited the Lei reference herein. Examiner notes for the record that the Lei et reference was properly cited on the PTO892 form provided to Applicant in the previous Office action mailed 9/22/2006.

Conclusion

No claim is allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571)

272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Joseph Woitach can be reached at (571) 272-0739.

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Patent Examiner
Art Unit 1636

May 2, 2007

DAVID GUZO
PRIMARY EXAMINER